IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE HONORABLE BOARD
OF PATENT APPEALS AND INTERFERENCES

In re the Application of Peter K. Law
Application No.: 09/005,034
Filed: January 9, 1998
Docket No.: 038007/0111
For: Myoblast Therapy for Cosmetic Treatment

REPLY BRIEF

Appeal from Group 1642

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This brief responds the Examiner's Answer, mailed November 7, 2000. Appellant renews its request that the Board of Patent Appeals and Interferences reverse the Examiner's holding that the subject claims are invalid as failing to satisfy the enablement requirement under 35 U.S.C. § 112, first paragraph.

I. REQUEST FOR ORAL HEARING

Pursuant to 37 C.F.R. 1.194, Appellant concurrently submits a request for an oral hearing, which is filed concurrently herewith in a separate sheet of paper, along with the appropriate fee.

II. OVERVIEW

A. The Dispositive Issue

The dispositive issue is that the PTO has not met its burden of alleging a sustainable *prima facie* case of non-enablement and that the Examiner's reliance on the applied references is unreasonable.

In order to make a rejection on enablement grounds, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. MPEP § 2164.04, citing *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). In this appeal, the Examiner relies on various prior art references, in an attempt to meet her burden. In response to the reasons set forth in the Examiner's Answer, Appellant submits that the Examiner has failed to meet the burden for demonstrating non-enablement.

B. Summary of Appellant's Primary Argument

Appellants' primary argument is summarized as follows:

- The Examiner has not met the burden of establishing a *prima facie* case of non-enablement, since the references on which the Examiner relies do not disprove the presumption of enablement to which the pending claims are entitled.

III. APPELLANT'S PRIMARY ARGUMENT

A. Statement of the Law on Enablement

1. According to MPEP § 2164.04 the Examiner has the initial burden to establish a basis to question enablement and the basis must be reasonable

The Examiner has the initial burden to establish a *reasonable* basis to question the enablement provided for the claimed invention when making a rejection under 35 U.S.C. § 112, first paragraph. *See In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). A specification disclosure that contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. MPEP § 2164.04 (July 1998). In other words, if the art reasonably does not cast doubt on the teachings of the claimed invention, then the Examiner properly may not reject the claims on enablement grounds.

B. Assertions Relating to Appellant's Primary Argument

This section rebuts the Examiner's assertions relating to Appellants' primary argument, which is summarized as follows:

> ➢ The Examiner has not met the burden of establishing a *prima facie* case of non-enablement, since the references on which the Examiner relies do not disprove the presumption of enablement to which the pending claims are entitled.

The Examiner cites four publications in attempting to sustain the PTO's burden of proving that the appealed claims are not enabled by the specification. These publications do not support a finding of non-enablement, however, since the Examiner's reliance on them is unreasonable.

1. *The Examiner's reliance on Coovert et al. is unreasonable because the present specification belies the key assertions by Coovert*

The Examiner cites Coovert *et al.*, "Gene therapy for muscle diseases," *Curr. Op. Neurobiol.* 7: 463-70 (1994), for the proposition that myoblast transfer in humans has not been successful (Examiner's Answer at page 5, lines 13-20). For several reasons, however, the Examiner's reliance on Coovert *et al.* is ill-founded.

First, the Examiner improperly applies the "silence" of Coovert *et al.* as evidence that the instant disclosure does not enable the claims. For instance, the Examiner states:

> [T]he art [] does not teach any resulting alteration in the 'cosmetic appearance' of the injected muscle or of the mouse [injected with myoblasts].

Thus, an accurate paraphrasing of the Examiner's reasoning is that, "since Coovert *et al.* do not teach that the present invention *is* enabled, then the present invention must *not* be enabled." According to this reasoning, it becomes incumbent upon an applicant to prove affirmatively that an invention is enabled when an applied reference does not state that a skilled worker *can* practice the invention, as claimed. This reasoning plainly illustrates how the Examiner improperly has shifted the burden on Appellant to prove that the claims are enabled.

The Examiner's reliance on Coovert *et al.* also is unreasonable because Coovert *et al.* never investigated the "cosmetic alteration" embodiment of the invention. For instance, Coovert *et al.* disclose, albeit quite cryptically, that myoblast transfer in humans suffering from muscular dystrophy has not been successful. Yet Coovert *et al.* do not speak of myoblast transfer in non-diseased muscle. Accordingly, Coovert *et al.* would not have been investigating, or otherwise interested in, whether "cosmetic alteration" occurred in the injected muscle. Moreover, to the extent that the Examiner relies on data from Coovert *et al.* relating to diseased muscle to reject the claims in question, Appellant already has shown that myoblast transfer therapy according to the present invention does work in diseased muscle (Specification at page 12, lines 16-31. Thus, the cited assertions of Coovert *et al.* provide no reasonable basis whatsoever for challenging the enabling quality of Appellant's specification, *vis-à-vis* the appealed claims.

Lastly, the Examiner cites Coovert *et al.* for the proposition that "injected myoblasts contribute to the formation of new muscle *in vivo* by fusing with endogenous myoblasts" (Examiner's Answer at page 6, lines 7-8). However, this portion of Coovert *et al.* merely reaffirms the teachings of the present invention. Indeed, the specification provides, "[i]njected muscles include those in the neck, shoulder, back, chest, abdomen, arms, hips, and legs" (Specification at page 12, lines 10-12). Appellant previously submitted that there is muscle tissue in the breast, as well as areas proximate the hip bone, with which administered myoblasts can fuse. Yet, by maintaining this rejection, the Examiner seems to ignore Appellant's teachings in this regard.

The Examiner apparently does not believe that injected myoblasts could interact with muscle cells in the respective tissues, stating, "human breast is composed of adipose tissue and the human hip is composed of bone" (Examiner's Answer at page 6, lines 5-6). The specification is clear, however, that administered myoblasts are to fuse with the *muscle* in these tissues. Further, conventional wisdom show that (1) human breast contains muscle tissue and (2) there is muscle tissue proximate to the hip bone with which administered myoblasts are capable of interacting. Accordingly, Coovert *et al.* does not oppose the teachings of the present invention in this context.

2. *Morgan et al. do not teach that injection of myoblasts into live muscle leads to tumor formation*

The Examiner relies on Morgan *et al.*, "Formation of skeletal muscle *in vivo* from the mouse C2 cell line," *J. Cell Sci.* 102: 779-87 (1992), to contend that "the art teaches that injection of proliferating undifferentiated muscle cells results in the formation of tumors at the sight of injection (Examiner's Answer at page 7, lines 2-4). According to Morgan *et al.*, however, tumor formation only occurs in certain limited instances. In fact, Morgan *et al.* only teach that tumor formation readily occurs when myoblasts are administered to freeze-killed muscle:

> although tumours of C2 origin were almost invariably found in older freeze-killed muscle grafts, they rarely formed tumours in live muscle autografts.

Accordingly, Morgan *et al.* do not teach that tumor formation occurs at the site of injection, after administering myoblasts to living muscle tissue.

The present invention does not require the administering of myoblasts to freeze-killed muscle. In fact, administered myoblasts would need to interact with live muscle (as opposed to freeze-killed muscle) to obtain a "cosmetic alteration" in a patient, according to the present invention. Thus Morgan *et al.* do not teach that this aspect of the invention is not enabled. Even Morgan *et al.*, themselves, show that there is no correlation between tumor formation in freeze-killed and living muscle tissues. Thus, the Examiner has failed to meet a burden of proving non-enablement in this context.

The teachings of Hoffman, *infra*, further undermine the Examiner's position on this point. Appellant discusses this aspect of Hoffman in the second paragraph of the following section.

3. *The Examiner's reliance on Hoffman is unreasonable inasmuch as Appellant does not bear the burden of proof when the applied publication is silent on issue(s) salient to enablement*

The Examiner cites Hoffman, "Myoblast Transplantation: What's Going On?" *Cell Trans.* 2: 49-57 (1993), concurrently with Coovert *et al.*, *supra,* for the proposition that "[the art] does not teach any resulting alteration in the 'cosmetic appearance' of the injected muscle or of the mouse [injected with myoblasts]" (*See* Examiner's Answer at page 5, lines 18-20). As indicated, the Examiner is stating, in effect, that "since Hoffman does not teach that the present invention *is* enabled, then the present invention must *not* be enabled." Clearly, Hoffman relates to myoblast transfer in patients suffering from musculature disorders and, hence, was not investigating the possibility of "cosmetic alteration" in these patients. For essentially the same reasons as set forth above, the Examiner's reasoning is wholly improper; again, Appellant does not bear the burden of proving enablement.

Hoffman also calls into serious question the Examiner's reliance on Morgan *et al.* as evidence that myoblast therapy can result in the formation of tumors at the site of injection. For instance, Hoffman states,

> "[w]hile no such tumors have been observed in humans to date [who have been administered myoblasts], the possibility clearly exists" (Hoffman at p. 54, right col.).

Thus, even the Hoffman reference, which takes a pragmatic approach to assessing the viability of myoblast transplantation, acknowledges that tumor formation does not readily occur in humans at the site of injection.

4. ***DiMario et al. never observe that myoblast transfer fails to work in non-diseased muscle, but instead conclude only that growing musculature responds to myoblast transfer to a lesser extent than regenerating muscle***

The Examiner cites DiMario *et al.* to support that the instant specification adequately does not teach *how* donor myoblasts could be used to alter the cosmetic appearance of non-diseased muscle (*See* Examiner's Answer at page 6, lines 14-18; page 9, lines 3-6). However, this line of reasoning fails show non-enablement of the present invention in at least two respects.

First, DiMario *et al.* never state that myoblast transfer would not work with non-diseased muscle. Instead, DiMario *et al.* provide only that "regenerating muscle provides a *better* environment for myoblast transfer and incorporation into new and existent muscle fibers than growing musculature..." (DiMario *et al.* at page 333, right col.). Thus, DiMario *et al.* do not rule out that myoblast transfer in non-diseased muscle can occur. The fact that an embodiment falling within the scope of the claims (*e.g.*, myoblast transfer to non-diseased muscle) has been obtained only in small amounts does not mean that the claimed invention is unpredictable or non-enabled. *See In re Wands,* 858 F.2d 731, 736, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). Thus, this disclosure of Dimario *et al.* is not sufficient to support a finding of non-enablement.

Furthermore, the conclusions of DiMario *et al.* are not indicative of the success of myoblast transfer according to the present invention, since the present invention discloses

enhanced methods of myoblast transfer to a patient. Indeed, the protocols that DiMario *et al.* disclose involve a much smaller concentration of myoblasts than in the protocols taught in the present invention. For instance, Dimario *et al.* refer to the work of Morgan *et al., supra*, when discussing these differing results between myoblast transfer in diseased and non-diseased muscle. Morgan *et al.* only disclose the administration of a maximum of 10^6 (*i.e.* 1 million) muscle precursor cells to a subject.

The present invention, on the other hand, teaches the administration of 12.5 billion myoblasts (*see* specification at page 12, line 8) and even discloses the "feasibility and safety in administering 30 billion myoblasts into a human subject..." (*Id.* at lines 32-33). Accordingly, the conclusions in DiMario *et al.* are not indicative of the expected results surrounding the present invention. Thus, the present invention's teachings reasonably would lead a skilled worker to expect results different than those disclosed in Dimario *et al.*

IV. CONCLUSIONS

In view of the foregoing, it is apparent that PTO has not met its burden of asserting a *prima facie* case of non-enablement that is sustainable. The foregoing arguments plainly illustrate how none of the applied references can substantiate the Examiner's position. Accordingly, Appellant respectfully solicits the Honorable Board of Patent Appeals and Interferences to reverse the rejection of the claims and pass this application on to allowance.

Respectfully submitted,

8 January 2001
Date

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